PATENTS

IN THE UNITED STATES PATENT AND TRADMARK OFFICE

Applicant: Judith Friese et al.	Attorney Docket No.: 7098.US.01
Serial No.: 10/620,475	Examiner: Ralph Gitomer
Filed: July 16, 2003	Art Unit: 1657
For: Stable Calibrators or Controls for Measuring Human Natriuretic Peptides	

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION TO WITHDRAW TERMINAL DISCLAIMERS

Dear Sir or Madam:

Applicants hereby petition under 37 C.F.R. § 1.182 for withdrawal of the two terminal disclaimers previously filed in the above-identified application.

Facts Supporting Withdrawal of Two Terminal Disclaimers

Applicants' understanding of events is as follows:

1. Claims 1, 2, 4-17 and 19-36 and 52 of the subject application are currently pending [copy included as **Appendix A**].

2. The two terminal disclaimers were filed in the subject application on April 25, 2007 to overcome the rejection of claims 1, 2, 3-17, 19-36, 52 and 53 of this application on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-36 of copending Application No. 10/721,031 (7098USP1) [copy of claims pending in Application No. 10/721,031 (7098USP1) at time of application of double patenting rejection in subject application included as **Appendix B**], and over claims 1-36 of co-pending application 11/248,650 (7098USC1) [copy of claims pending in 11/248,650 (7098USC1) at time of application of double patenting rejection in subject application included as **Appendix C**].

3. With regard to co-pending Application No. 11/248,650 (7098USC1), the overlapping claims 1-36 of 11/248,650 (7098USC1) have been cancelled. Claims 37-51 are currently pending [copy included as **Appendix D**].

4. The co-pending Application No. 11/248,650 (7098USC1) was recently determined to be a divisional of the current application, and not a continuation application, as had been previously stated. A requirement for restriction was imposed April 24, 2006 in Application No. 11/248,650 (7098USC1), requiring election of the claims of either Group I

(claims 1-36) or Group II (Claims 37-51). However, this requirement merely reiterated the requirement for restriction that was earlier imposed on December 22, 2005 in the subject (parent) application, requiring election of the claims of either Group I (claims 1-17 and 19-36; claim 18 having been canceled) or Group II (Claims 37-51).

5. With regard to co-pending Application No. 10/721,031 (7098USP1), the overlapping claims 1-36 of Application No. 10/721,031 (7098USP1) have been cancelled. Claims 95-106 have been allowed [copy included as **Appendix E**].

6. The co-pending Application No. 10/721,031 (7098USP1) is a later-filed continuation-in-part application of the subject application. The allowed claims are directed to subject matter that differs from that of the subject application and was newly added in the continuation-in-part (e.g., stable ***test samples*** versus stable calibrators or controls). Applicants respectfully submit that the allowed claims of Application No. 10/721,031 (7098USP1) have not been considered as unpatentable for nonstatutory obviousness-type double patenting over the claims of the subject application by Examiner Gitomer.

Legal Basis Supporting Withdrawal of Two Terminal Disclaimers

7. Pursuant to paragraphs 2-4 above, the election of differing claims in Application No. 11/248,650 (7098USC1) and the subject application, and the creation of the divisional relationship between the applications, was done in response to a restriction requirement, and not of applicants' own accord. The relationship between these applications had previously been incorrectly cited, but was recently amended to correctly recite that of a divisional application and its parent. 35 U.S.C. § 121 generally prohibits a double patenting rejection where the claimed subject matter is presented in a divisional application as a result of a restriction requirement. On this basis of this erroneous filing of the terminal disclaimer over claims in Application No. 11/248,650 (7098USC1), applicants request withdrawal of this terminal disclaimer.

8. Pursuant to paragraphs 5-6 above, election of differing claims in Application No. 10/721,031 (7098USP1) and the different subject matter of this application as compared to the subject application support that the double patenting rejection was unwarranted, and that the terminal disclaimer should not have been filed. On this basis of this erroneous filing, applicants request withdrawal of the terminal disclaimer over Application No. 10/721,031 (7098USP1) filed in response to this rejection.

9. Pursuant to paragraphs 1-6 above, there appears to be no overlap between the claims of the subject application with those of Application Nos. 11/248,650 (7098USC1) or 10/721,031 (7098USP1) such as would warrant a terminal disclaimer. Applicants undersigned counsel admits that this should have been recognized and the foregoing arguments should have been presented at the time the terminal disclaimers were filed, instead of filing the terminal disclaimers. On this basis of this erroneous filing, applicants request withdrawal of the terminal disclaimers over Application Nos. 11/248,650 (7098USC1) and 10/721,031 (7098USP1) filed in response to this rejection.

10. There is no statutory prohibition against nullifying or otherwise canceling the effect of a recorded terminal disclaimer that was erroneously filed before a patent issues. *Manual of Patent Examining Procedure*, § 1490, page 1400-114 (Online, § 14.38), Eighth Edition, August 2001; Latest Revision August 2006. Because a terminal disclaimer does not take effect

until a patent is granted, the public has not had the opportunity to rely on the terminal disclaimer. *Id.* Thus, withdrawal of the erroneous filing of a terminal disclaimer may be available by way of petition prior to patent issuance. *Id.*

Absence of Delay

11. Applicants' undersigned counsel submits that this Petition is being filed diligently without delay. Applicants filed a response requesting withdrawal of the terminal disclaimers on June 1, 2007, immediately upon realizing the erroneous nature of the terminal disclaimer filings.

12. Applicants' undersigned counsel received a voice message from Examiner Gitomer on August 20, 2007 suggesting that the request for withdrawal be done by way of Petition, and is promptly filing this Petition.

13. Applicants' undersigned counsel regrets not raising these arguments earlier, as well as the error made in the filing of the terminal disclaimers, and requests that these arguments be considered now, in view of the claims which have been selected for prosecution in these related applications. Based on the foregoing, Applicants hereby petition the Commissioner for Patents to withdraw the terminal disclaimers under 37 CFR § 1.182.

CONCLUSION

Based on the foregoing, Applicants hereby petition the Commissioner of Patents and Trademarks to withdraw the terminal disclaimers referenced above.

In the event that this petition is not granted, and in view of the fact that terminal disclaimers were not filed in Application Nos. 11/248,650 (7098USC1) and 10/721,031 (7098USP1), Applicants acknowledge that the filing of a terminal disclaimer to obviate a rejection based on nonstatutory double patenting is not an admission of the propriety of the rejection but simply serves the statutory function of removing the rejection of double patenting.

Respectfully submitted,
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APPENDIX A - CURRENTLY PENDING CLAIMS OF 7098US01
(Claims as amended April 25, 2007)

1. (Previously Presented). A stable liquid calibrator or control for use in a ligand binding assay for measuring a level of a natriuretic peptide in a test sample, wherein said calibrator or control comprises at least one human synthetic natriuretic peptide, has a pH of from about 4.0 to about 6.5, and remains stable when stored at temperatures of from about 2 to about 8°C for a period of about twelve (12) months.

2. (Original). The calibrator or control of claim 1, wherein said calibrator or control has a pH of from about 5.0 to about 6.0.

3. (Canceled).

4. (Currently Amended). The calibrator or control of claim 1, wherein said human synthetic natriuretic peptide is selected from the group consisting of human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide [[or]] and human synthetic *Dendroaspsis* natriuretic peptide.

5. (Original). The calibrator or control of claim 1, wherein said calibrator or control comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

6. (Currently Amended). The calibrator or control of claim 5, wherein said buffer is selected from the group consisting of an acetate buffer, a citrate buffer, a phosphate buffer [[or]] and combinations thereof.

7. (Currently Amended). The calibrator or control of claim 5, wherein said acid is selected from the group consisting of acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid [[or]] and combinations thereof.

8. (Original). The calibrator or control of claim 5, wherein the base is sodium hydroxide.

9. (Original). The calibrator or control of claim 1, wherein said calibrator or control comprises at least one diluent.

10. (Original). The calibrator or control of claim 9, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

11. (Original). The calibrator or control of claim 10, wherein said natriuretic stabilizing compound is a protein or a polymer.

12. (Currently Amended). The calibrator or control of claim 11, wherein the protein is selected from the group consisting of bovine serum albumin, bovine gamma globulin, [[or]] and a non-fat dry milk.

13. (Currently Amended). The calibrator or control of claim 11, wherein the polymer is selected from the group consisting of polyethylene glycol, dextran, dextran sulfate [[or]] and polyvinyl pyrrolidone.

14. (Original). The calibrator or control of claim 9, wherein the diluent further comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

15. (Currently Amended). The calibrator or control of claim 14, wherein said buffer is selected from the group consisting of an acetate buffer, a citrate buffer, a phosphate buffer [[or]] and combinations thereof.

16. (Currently Amended). The calibrator or control of claim 14, wherein said acid is selected from the group consisting of acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid [[or]] and combinations thereof.

17. (Original). The calibrator or control or claim 14, wherein the base is sodium hydroxide.

18. (Canceled).

19. (Original). The calibrator or control of claim 1, wherein said calibrator or control can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40 °C.

20. (Previously Presented). A stable liquid calibrator or control for use in a ligand binding assay for measuring a level of natriuretic peptide in a test sample, wherein said calibrator or control comprises:

at least one diluent; and

at least one human synthetic natriuretic peptide,

wherein said calibrator or control has a pH of from about 4.0 to about 6.5, and

wherein the calibrator or control remains stable when stored at temperatures of from about 2 to about 8°C for a period of about twelve (12) months.

21. (Original). The calibrator or control of claim 20, wherein said calibrator or control has a pH of from about 5.0 to about 6.0.

22. (Currently Amended). The calibrator or control of claim 20, wherein said human synthetic natriuretic peptide is selected from the group consisting of human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide [[or]] and human synthetic *Dendroaspsis* natriuretic peptide.

23. (Original). The calibrator or control of claim 20, wherein said calibrator or control comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

24. (Currently Amended). The calibrator or control of claim 23, wherein said buffer is selected from the group consisting of an acetate buffer, a citrate buffer, a phosphate buffer [[or]] and combinations thereof.

25. (Currently Amended). The calibrator or control of claim 23, wherein said acid is selected from the group consisting of acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid [[or]] and combinations thereof.

26. (Original). The calibrator or control of claim 23, wherein the base is sodium hydroxide.

27. (Original). The calibrator or control of claim 20, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

28. (Original). The calibrator or control of claim 27, wherein said natriuretic stabilizing compound is a protein or a polymer.

29. (Currently Amended). The calibrator or control of claim 28, wherein the protein is selected from the group consisting of bovine serum albumin, bovine gamma globulin, [[or]] and a non-fat dry milk.

30. (Currently Amended). The calibrator or control of claim 28, wherein the polymer is selected from the group consisting of polyethylene glycol, dextran, dextran sulfate [[or]] and polyvinyl pyrrolidone.

31. (Original). The calibrator or control of claim 27, wherein the diluent further comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

32. (Currently Amended). The calibrator or control of claim 31, wherein said buffer is selected from the group consisting of an acetate buffer, a citrate buffer, a phosphate buffer [[or]] and combinations thereof.

33. (Currently Amended). The calibrator or control of claim 31, wherein said acid is selected from the group consisting of acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid [[or]] and combinations thereof.

34. (Original). The calibrator or control or claim 31, wherein the base is sodium hydroxide.

35. (Original). The calibrator or control of claim 20, wherein said calibrator or control can be stored at a temperature of from about 2 to about 8 °C.

36. (Original). The calibrator or control of claim 20, wherein said calibrator or control can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40 °C.

37. – 51 (Canceled).

52. (Currently Amended). A stable liquid calibrator or control for use in a ligand binding assay for measuring a level of a natriuretic peptide in a test sample, wherein said calibrator or control comprises at least one human synthetic natriuretic peptide, has a pH of from about 4.0 to about 6.5~~, is not reconstituted from a lyophilisate,~~ and is reusable.

53. (Canceled).

APPENDIX B - Copy Of Claims Pending In Application No. 10/721,031 (7098USP1) At Time Of Application Of Double Patenting Rejection In Subject Application (Claims as Originally Filed)

1. A stable liquid calibrator or control for use in a ligand binding assay for measuring the level of a natriuretic peptide in a test sample, wherein said calibrator or control has a pH of from about 4.0 to about 6.5.

2. The calibrator or control of claim 1, wherein said calibrator or control has a pH of from about 5.0 to about 6.0.

3. The calibrator or control of claim 1, wherein said calibrator or control comprises at least one human synthetic natriuretic peptide.

4. The calibrator or control of claim 3, wherein said human synthetic natriuretic peptide is human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide or human synthetic *Dendroaspis* natriuretic peptide.

5. The calibrator or control of claim 1, wherein said calibrator or control comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

6. The calibrator or control of claim 5, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

7. The calibrator or control of claim 5, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

8. The calibrator or control of claim 5, wherein the base is sodium hydroxide.

9. The calibrator or control of claim 1, wherein said calibrator or control comprises at least one diluent.

10. The calibrator or control of claim 9, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

11. The calibrator or control of claim 10, wherein said natriuretic stabilizing compound is a protein or a polymer.

12. The calibrator or control of claim 11, wherein the protein is bovine serum albumin, bovine gamma globulin, or a non-fat dry milk.

13. The calibrator or control of claim 11, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

14. The calibrator or control of claim 9, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

15. The calibrator or control of claim 14, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

16. The calibrator or control of claim 14, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

17. The calibrator or control of claim 14, wherein the base is sodium hydroxide.

18. The calibrator or control of claim 1, wherein said calibrator or control can be stored at a temperature of from about 2 to about 8°C.

19. The calibrator or control of claim 1, wherein said calibrator or control can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40°C.

20. A stable liquid calibrator or control for use in a ligand binding assay for measuring the level of a natriuretic peptide in a test sample, wherein said calibrator or control comprises:

at least one diluent; and

at least one human synthetic natriuretic peptide,

wherein said calibrator or control has a pH of from about 4.0 to about 6.5.

21. The calibrator or control of claim 20, wherein said calibrator or control has a pH of from about 5.0 to about 6.0.

22. The calibrator or control of claim 20, wherein the human synthetic natriuretic peptide is human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide or human synthetic *Dendroaspis* natriuretic peptide.

23. The calibrator or control of claim 20, wherein said calibrator or control further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

24. The calibrator or control of claim 23, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

25. The calibrator or control of claim 23, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

26. The calibrator or control of claim 23, wherein the base is sodium hydroxide.

27. The calibrator or control of claim 20, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

28. The calibrator or control of claim 27, wherein said natriuretic stabilizing compound is a protein or a polymer.

29. The calibrator or control of claim 28, wherein the protein is bovine serum albumin, a bovine gamma globulin, or a non-fat dry milk.

30. The calibrator or control of claim 28, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

31. The calibrator or control of claim 27, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

32. The calibrator or control of claim 31, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

33. The calibrator or control of claim 31, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

34. The calibrator or control of claim 31, wherein the base is sodium hydroxide.

35. The calibrator or control of claim 20, wherein said calibrator or control can be stored at a temperature of from about 2 to about 8°C.

36. The calibrator or control of claim 20, wherein said calibrator or control can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40°C.

37. A method of making a stable liquid calibrator or control for use in a ligand binding assay for measuring the level of a natriuretic peptide in a test sample, wherein the method comprises the steps of:

a. mixing at least one diluent with at least one human synthetic natriuretic peptide to form a liquid calibrator or control;

b. measuring the pH of the liquid calibrator or control; and

c. depending upon the pH of the liquid calibrator or control measured in step b), adjusting the pH of the liquid calibrator or control to a pH of from about 4.0 to about 6.5.

38. The method of claim 37, wherein the pH of the liquid calibrator or control is adjusted to a pH of from about 5.0 to about 6.0.

39. The method of claim 37, wherein the human synthetic natriuretic peptide is human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide or human synthetic *Dendroaspis* natriuretic peptide.

40. The method of claim 37, wherein the pH of the liquid calibrator or control is adjusted with at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

41. The method of claim 40, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

42. The method of claim 40, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

43. The method of claim 40, wherein the base is sodium hydroxide.

44. The method of claim 37, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

45. The method of claim 44, wherein said natriuretic stabilizing compound is a protein or a polymer.

46. The method of claim 45, wherein the protein is bovine serum albumin, bovine gamma globulin, or a non-fat dry milk.

47. The method of claim 45, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

48. The method of claim 44, wherein the diluent further comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

49. The method of claim 48, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

50. The method of claim 48, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

51. The method of claim 48, wherein said base is sodium hydroxide.

52. A stable test sample for use in a ligand binding assay for measuring the level of a natriuretic peptide in said test sample, wherein said test sample comprises a pH of from about 4.0 to about 6.5.

53. The test sample of claim 52, wherein said test sample comprises at least one human natural natriuretic peptide.

54. The test sample of claim 53, wherein said human natural natriuretic peptide is human natural atrial natriuretic peptide, human natural B-type natriuretic peptide, human natural C-type natriuretic peptide or human natural *Dendroaspis* natriuretic peptide.

55. The test sample of claim 52, wherein said test sample comprises at least one diluent.

56. The test sample of claim 55, wherein said diluent has a pH of from about 4.0 to about 6.0.

57. The test sample of claim 56, wherein said diluent has a pH of from about 5.4 to about 5.6.

58. The test sample of claim 55, wherein said test sample comprises from about 5% to about 95% (v/v) of a diluent.

59. The test sample of claim 58, wherein said test sample comprises from about 20% to about 90% (v/v) of a diluent.

60. The test sample of claim 55, wherein said diluent comprises at least one natriuretic stabilizing compound.

61. The test sample of claim 60 wherein said natriuretic stabilizing compound is a protein or a polymer.

62. The test sample of claim 61, wherein the protein is bovine serum albumin, bovine gamma globulin, or a non-fat dry milk.

63. The test sample of claim 61, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

64. The test sample of claim 60, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

65. The test sample of claim 64, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

66. The test sample of claim 64, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

67. The test sample of claim 64, wherein the base is sodium hydroxide.

68. The test sample of claim 52, wherein said test sample can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40°C.

69. A stable test sample for use in a ligand binding assay for measuring the level of a natural natriuretic peptide in said test sample sample, wherein said test sample comprises:

from about 5% to about 95% (v/v) of at least one diluent; and

at least one biological sample derived from serum, plasma, whole blood or other bodily fluid that contains at least one natriuretic peptide,

wherein said test sample has a pH of from about 4.0 to about 6.5.

70. The test sample of claim 69, wherein said diluent has a pH of from about 5.0 to about 6.0.

71. The test sample of claim 70 wherein the diluent has a pH of from about 5.4 to about 5.6.

72. The test sample of claim 69, wherein the test sample comprises from about 20% to about 90% (v/v) of at least one diluent.

73. The test sample of claim 69, wherein the human natural natriuretic peptide is human natural atrial natriuretic peptide, human natural B-type natriuretic peptide, human natural C-type natriuretic peptide or human natural *Dendroaspis* natriuretic peptide.

74. The test sample of claim 69, wherein said diluent comprises at least one natriuretic stabilizing compound.

75. The test sample of claim 74, wherein said natriuretic stabilizing compound is a protein or a polymer.

76. The test sample of claim 75, wherein the protein is bovine serum albumin, a bovine gamma globulin, or a non-fat dry milk.

77. The test sample of claim 75, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

78. The test sample of claim 69, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

79. The test sample of claim 78, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

80. The test sample of claim 78, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

81. The test sample of claim 78, wherein the base is sodium hydroxide.

82. The test sample of claim 69, wherein said test sample can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40°C.

83. A method of making a stable, test sample for use in a ligand binding assay for measuring the level of a natriuretic peptide in said test sample, wherein the method comprises the step of:

mixing from about 5% to about 95% (v/v) of at least one diluent having a pH of from about 4.0 to about 6.0 with at least one biological sample derived from serum, plasma, whole blood or other bodily fluids and that contains at least one natriuretic peptide, to form a stable test sample having a pH from about 4.0 to about 6.5.

84. The method of claim 83, wherein the natural natriuretic peptide is human natural atrial natriuretic peptide, human natural B-type natriuretic peptide, human natural C-type natriuretic peptide or human natural *Dendroaspis* natriuretic peptide.

85. The method of claim 83, wherein from about 70% to about 90% (v/v) of a diluent is mixed with at least one biological sample.

86. The method of claim 83, wherein the diluent has a pH of from about 5.4 to about 5.6.

87. The method of claim 83, wherein said diluent comprises at least one natriuretic stabilizing compound.

88. The method of claim 87, wherein said natriuretic stabilizing compound is a protein or a polymer.

89. The method of claim 88, wherein the protein is bovine serum albumin, bovine gamma globulin, or a non-fat dry milk.

90. The method of claim 88, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

91. The method of claim 83, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base.

92. The method of claim 91, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

93. The method of claim 91, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

94. The method of claim 91, wherein said base is sodium hydroxide.

95. A method of stabilizing a test sample for use in a ligand binding assay for measuring the level of a natriuretic peptide in said test sample, wherein the method comprises the step of:

mixing from about 5% to about 95% (v/v) of at least one diluent having a pH of from about 4.0 to about 6.0 with at least one biological sample derived from serum, plasma, whole blood or other bodily fluids and that contains at least one natriuretic peptide, to form a stablilized test sample having a pH from about 4.0 to about 6.5.

96. The method of claim 95, wherein the natural natriuretic peptide is human natural atrial natriuretic peptide, human natural B-type natriuretic peptide, human natural C-type natriuretic peptide or human natural *Dendroaspis* natriuretic peptide.

97. The method of claim 95, wherein from about 70% to about 90% (v/v) of a diluent is mixed with at least one biological sample.

98. The method of claim 95, wherein the diluent has a pH of from about 5.4 to about 5.6.

99. The method of claim 95, wherein said diluent comprises at least one natriuretic stabilizing compound.

100. The method of claim 99, wherein said natriuretic stabilizing compound is a protein or a polymer.

101. The method of claim 100, wherein the protein is bovine serum albumin, bovine gamma globulin, or a non-fat dry milk.

102. The method of claim 100, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

103. The method of claim 95, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base .

104. The method of claim 103, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

105. The method of claim 103, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

106. The method of claim 103, wherein said base is sodium hydroxide.

APPENDIX C - Copy Of Claims Pending In 11/248,650 (7098USC1) At Time Of Application Of Double Patenting Rejection In Subject Application
(Claims as originally filed)

1. A stable liquid calibrator or control for use in a ligand binding assay for measuring the level of a natriuretic peptide in a test sample, wherein said calibrator or control has a pH of from about 4.0 to about 6.5.

2. The calibrator or control of claim 1, wherein said calibrator or control has a pH of from about 5.0 to about 6.0.

3. The calibrator or control of claim 1, wherein said calibrator or control comprises at least one human synthetic natriuretic peptide.

4. The calibrator or control of claim 3, wherein said human synthetic natriuretic peptide is human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide or human synthetic *Dendroaspis* natriuretic peptide.

5. The calibrator or control of claim 1, wherein said calibrator or control comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

6. The calibrator or control of claim 5, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

7. The calibrator or control of claim 5, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

8. The calibrator or control of claim 5, wherein the base is sodium hydroxide.

9. The calibrator or control of claim 1, wherein said calibrator or control comprises at least one diluent.

10. The calibrator or control of claim 9, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

11. The calibrator or control of claim 10, wherein said natriuretic stabilizing compound is a protein or a polymer.

12. The calibrator or control of claim 11, wherein the protein is bovine serum albumin, bovine gamma globulin, or a non-fat dry milk.

13. The calibrator or control of claim 11, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

14. The calibrator or control of claim 9, wherein the diluent further comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

15. The calibrator or control of claim 14, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

16. The calibrator or control of claim 14, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

17. The calibrator or control of claim 14, wherein the base is sodium hydroxide.

18. The calibrator or control of claim 1, wherein said calibrator or control can be stored at a temperature of from about 2 to about 8°C.

19. The calibrator or control of claim 1, wherein said calibrator or control can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40°C.

20. A stable liquid calibrator or control for use in a ligand binding assay for measuring the level of a natriuretic peptide in a test sample, wherein said calibrator or control comprises:

at least one diluent; and

at least one human synthetic natriuretic peptide,

wherein said calibrator or control has a pH of from about 4.0 to about 6.5.

21. The calibrator or control of claim 20, wherein said calibrator or control has a pH of from about 5.0 to about 6.0.

22. The calibrator or control of claim 20, wherein the human synthetic natriuretic peptide is human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide or human synthetic *Dendroaspis* natriuretic peptide.

23. The calibrator or control of claim 20, wherein said calibrator or control further comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

24. The calibrator or control of claim 23, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

25. The calibrator or control of claim 23, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

26. The calibrator or control of claim 23, wherein the base is sodium hydroxide.

27. The calibrator or control of claim 20, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

28. The calibrator or control of claim 27, wherein said natriuretic stabilizing compound is a protein or a polymer.

29. The calibrator or control of claim 28, wherein the protein is bovine serum albumin, a bovine gamma globulin, or a non-fat dry milk.

30. The calibrator or control of claim 28, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

31. The calibrator or control of claim 27, wherein the diluent further comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

32. The calibrator or control of claim 31, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

33. The calibrator or control of claim 31, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

34. The calibrator or control of claim 31, wherein the base is sodium hydroxide.

35. The calibrator or control of claim 20, wherein said calibrator or control can be stored at a temperature of from about 2 to about 8°C.

36. The calibrator or control of claim 20, wherein said calibrator or control can be used in an assay at ambient temperature or at a temperature of from about 30 to about 40°C.

37. A method of making a stable liquid calibrator or control for use in a ligand binding assay for measuring the level of a natriuretic peptide in a test sample, wherein the method comprises the steps of:

a. mixing at least one diluent with at least one human synthetic natriuretic peptide to form a liquid calibrator or control;

b. measuring the pH of the liquid calibrator or control; and

c. depending upon the pH of the liquid calibrator or control measured in step b), adjusting the pH of the liquid calibrator or control to a pH of from about 4.0 to about 6.5.

38. The method of claim 37, wherein the pH of the liquid calibrator or control is adjusted to a pH of from about 5.0 to about 6.0.

39. The method of claim 37, wherein the human synthetic natriuretic peptide is human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide or human synthetic *Dendroaspis* natriuretic peptide.

40. The method of claim 37, wherein the pH of the liquid calibrator or control is adjusted with at least one buffer, at least one acid, at least one base, or combinations thereof.

41. The method of claim 40, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

42. The method of claim 40, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

43. The method of claim 40, wherein the base is sodium hydroxide.

44. The method of claim 37, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

45. The method of claim 44, wherein said natriuretic stabilizing compound is a protein or a polymer.

46. The method of claim 45, wherein the protein is bovine serum albumin, bovine gamma globulin, or a non-fat dry milk.

47. The method of claim 45, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

48. The method of claim 44, wherein the diluent further comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

49. The method of claim 48, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

50. The method of claim 48, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

51. The method of claim 48, wherein said base is sodium hydroxide.

APPENDIX D - Copy Of Current Claims In 11/248,650 (7098USC1)

(Claims as amended January 18, 2007)

1. – 36. (canceled)

37. (amended) A method of making a stable liquid calibrator or control for use in a ligand binding assay for measuring [[the]] a level of a natriuretic peptide in a test sample, wherein the method comprises the steps of:

a. mixing at least one diluent with at least one human synthetic natriuretic peptide to form a liquid calibrator or control;

b. measuring [[the]] a pH of the liquid calibrator or control; and

c. depending upon the pH of the liquid calibrator or control measured in step b), adjusting the pH of the liquid calibrator or control to a pH of from about 4.0 to about 6.5.

38. (original) The method of claim 37, wherein the pH of the liquid calibrator or control is adjusted to a pH of from about 5.0 to about 6.0.

39. (original) The method of claim 37, wherein the human synthetic natriuretic peptide is human synthetic atrial natriuretic peptide, human synthetic B-type natriuretic peptide, human synthetic C-type natriuretic peptide or human synthetic *Dendroaspis* natriuretic peptide.

40. (original) The method of claim 37, wherein the pH of the liquid calibrator or control is adjusted with at least one buffer, at least one acid, at least one base, or combinations thereof.

41. (original) The method of claim 40, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

42. (original) The method of claim 40, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

43. (original) The method of claim 40, wherein the base is sodium hydroxide.

44. (original) The method of claim 37, wherein said diluent comprises at least one natriuretic stabilizing compound and at least one biocide.

45. (original) The method of claim 44, wherein said natriuretic stabilizing compound is a protein or a polymer.

46. (original) The method of claim 45, wherein the protein is bovine serum albumin, bovine gamma globulin, or a non-fat dry milk.

47. (original) The method of claim 45, wherein the polymer is polyethylene glycol, dextran, dextran sulfate or polyvinyl pyrrolidone.

48. (original) The method of claim 44, wherein the diluent further comprises at least one buffer, at least one acid, at least one base, or combinations thereof.

49. (original) The method of claim 48, wherein said buffer is an acetate buffer, a citrate buffer, a phosphate buffer or combinations thereof.

50. (original) The method of claim 48, wherein said acid is acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid or combinations thereof.

51. (original) The method of claim 48, wherein said base is sodium hydroxide.

APPENDIX E - Copy Of Current Claims In 10/721,031 (7098USP1)
(Claims as amended April 24, 2007)

1. – 94. (Canceled)

95. (Currently Amended) A method of stabilizing a test sample for use in a ligand binding assay for measuring [[the]] a level of a natriuretic peptide in said test sample, wherein the method comprises the step of:

mixing from about 5% to about 95% (v/v) of at least one diluent having a pH of from about 4.0 to about 6.0 with at least one biological sample derived from serum, plasma, whole blood or other bodily fluids and that contains at least one natriuretic peptide, to form a stablilized test sample having a pH from about 4.0 to about 6.5.

96. (Currently Amended) The method of claim 95, wherein the ~~natural~~ natriuretic peptide is a natural peptide selected from the group consisting of human natural atrial natriuretic peptide, human natural B-type natriuretic peptide, human natural C-type natriuretic peptide [[or]] and human natural Dendroaspis natriuretic peptide.

97. (Original) The method of claim 95, wherein from about 70% to about 90% (v/v) of a diluent is mixed with at least one biological sample.

98. (Original) The method of claim 95, wherein the diluent has a pH of from about 5.4 to about 5.6.

99. (Original) The method of claim 95, wherein said diluent comprises at least one natriuretic stabilizing compound.

100. (Original) The method of claim 99, wherein said natriuretic stabilizing compound is a protein or a polymer.

101. (Currently Amended) The method of claim 100, wherein the protein is selected from the group consisting of bovine serum albumin, bovine gamma globulin, [[or]] and a non-fat dry milk.

102. (Currently Amended) The method of claim 100, wherein the polymer is selected from the group consisting of polyethylene glycol, dextran, dextran sulfate [[or]] and polyvinyl pyrrolidone.

103. (Original) The method of claim 95, wherein the diluent further comprises at least one buffer, or at least one acid, or at least one base, or combinations of at least one buffer, at least one acid and/or at least one base .

104. (Currently Amended) The method of claim 103, wherein said buffer is selected from the group consisting of an acetate buffer, a citrate buffer, a phosphate buffer [[or]] and combinations thereof.

105. (Currently Amended) The method of claim 103, wherein said acid is selected from the group consisting of acetic acid, citric acid, diethylenetriaminepentaacetic acid, hydrochloric acid [[or]] and combinations thereof.

106. (Original) The method of claim 103, wherein said base is sodium hydroxide.